

ABSTRACT

Due to the barrier imposed by the cell membrane, delivery of macromolecules in excess of 500 Daltons directly into cells remains problematic. However, proteins, which have been evolutionarily selected to perform specific functions, are therefore an attractive therapeutic agent to treat a variety of human diseases. In practice, the direct intracellular delivery of these proteins has, until recently, been difficult to achieve due primarily to the bioavailability barrier of the plasma membrane, which effectively prevents the uptake of the majority of peptides and proteins by limiting their passive entry. However, recent work using small cationic peptides, termed protein transduction domains (PTDs), derived from polynucleotide binding proteins, such as HIV TAT protein or the *Drosophila* transcription factor Antp. or synthetic poly-Arginine, have now been shown to deliver a myriad of molecules, including synthetic small molecules, peptides and proteins, into animal models *in vivo*.